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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,402	10/16/2003	Jaya Sivaswami Tyagi	AP35478 066123.0125	8618

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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/687,402	TYAGI ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 22-37 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 22-37 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 6, 2006, has been entered.

The amendment filed October 6, 2006, has been received and entered. Claims 1-21 are canceled. Claims 22-37 are new.

Applicant's election with traverse of the species wherein $DevS_{578}$ is the DevS derivative, $Rv2027_{194}$ is the Rv2027 derivative, and $DevRN_{145}$ is the DevR derivative, in the reply filed December 9, 2004, is acknowledged and applies to the new claims (claims 24, 26, 28, 29, 32, 34, 36, and 37).

Claims 22-37 are pending and examined on the merits to the extent they read on the elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as filed contains no limitations of the determination of the drug potential of the test compound wherein the potency of the drug is inversely proportional to "the degree of phosphotransfer" from "phosphorylated DevS to DevR" (claim 22), "phosphorylated single domain derivative of DevS to DevR" (claim 23), "phosphorylated DevS to a single domain derivative of DevR" (claim 25), "phosphorylated single domain derivative of DevS to a single domain derivative of DevR" (claim 27), "phosphorylated Rv2027c to DevR" (claim 30), "phosphorylated single domain derivative of Rv2027c to DevR" (claim 31), "phosphorylated Rv2027c to a single domain derivative of DevR" (claim 33), or "phosphorylated single domain derivative of Rv2027c to a single domain derivative of DevR" (claim 35). Instead, the disclosure indicates that the potency of the drug is inversely proportional to "the degree of phosphotransfer-based dephosphorylation of DevR and its single domain derivative" (page 25, paragraph [0059]), thus implying phosphotransfer from phosphorylated DevR, where the recipient(s) is not disclosed. The rate of dephosphorylation of phosphorylated species of species of DevS and Rv2027c do not speak to the degree of phosphotransfer to DevR, nor does Figure 9 or any reference to Figure 9 correlate phosphotransfer from DevS or Rv2027c to DevR to determinations of drug potency.

Additionally, the specification does not disclose the determination of the drug potential of the test compound wherein the potency of the drug is inversely proportional to "the degree of loss of phosphate-associated radioactivity" from "DevS or DevR in a reaction containing DevS and DevR" (claim 22), "a single domain derivative of DevS or DevR in a reaction containing a

single domain derivative of DevS and DevR" (claim 23), "DevS or a single domain derivative of DevR in a reaction containing DevS and a single domain derivative of DevR" (claim 25), "single domain derivative of DevS or a single domain derivative of DevR in a reaction containing a single domain derivative of DevS and a single domain derivative of DevR" (claim 27), "Rv2027c or DevR in a reaction containing Rv2027c and DevR" (claim 30), "a single domain derivative of Rv2027c or DevR in a reaction containing a single domain derivative of Rv2027c and DevR" (claim 31), "Rv2027c or a single domain derivative of DevR in a reaction containing Rv2027c and a single domain derivative of DevR" (claim 33), or "single domain derivative of Rv2027c or a single domain derivative of DevR in a reaction containing a single domain derivative of Rv2027c and a single domain derivative of DevR" (claim 35). Though paragraph [0178] indicates that in screening of inhibitors, "presence of a true inhibitor will not lead to reduction of retention of radioactivity on the filter," the specification does not specify that there is a clear relationship between drug potential and loss of phosphate-associated radioactivity. There is no teaching that any reduction of retention of radioactivity on the filter determines anti-mycobacterial drug potential. In sum, because the specification as filed fails to provide clear support for the new claim language, a new matter rejection is clearly proper.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoch et al. (US Patent 6,043,045) in view of Dasgupta et al. (2000, Tubercle and Lung Disease, 80(3): 141-159).

Hoch et al. discloses a method for identifying new antibiotic, antibacterial, or antimicrobial agents by inhibition of bacterial two-component systems. Specifically, agents are sought that cause the "inhibition of either the autophosphorylation or the subsequent phosphor-transfer" (column 2, lines 16-23). Furthermore, the conventional use of SDS-PAGE to assay two-component systems is described (column 2, lines 24-35), where autoradiographic analysis is used. Hoch et al. provides a high-throughput screening assay for histidine protein kinase for agent identification (column 22, lines 16-24), as described in Example 1 starting at lines 30 of column 15. In this high-throughput screening assay, the histidine protein kinase (KinA) and its substrate (SpoOF) are expressed in *E.coli* and purified (column 15, lines 45-47). This can be considered the overexpression of the histidine protein kinase. This high-throughput screening

assay measures the extent of phosphorylation of the substrate and the radioactivity remaining on a resin (column 2, lines 50-53 and column 17, lines 43-45) following SDS-PAGE analysis.

Hoch et al. does not expressly disclose the use of their methods for inhibition of DevR-DevS or DevR-Rv2027c and its homologues nor does it disclose the identification of anti-tuberculosis and anti-mycobacterial compounds. Additionally, Hoch et al. does not disclose the relation between the potency of a drug and the degree of phosphotransfer and loss of phosphate-associated radioactivity.

Dasgupta et al. discloses the DevR-DevS two-component system in mycobacteria, specifically *M. tuberculosis*, as well as the homology of Rv2027c with DevS. It is obvious that $DevS_{578}$, $Rv2027_{194}$, and $DevRN_{145}$ would share common characteristics with DevS, Rv2027 and DevR respectively because, as evidenced by Dasgupta (Figure 3, page 148 and Figure 5, page 150), the claimed portions each contain the catalytic site of the molecules, based on the size of the transcripts disclosed in the reference.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to apply the methods of Hoch et al. to the DevR-DevS and the known homolog of DevR-Rv2027c as described in Dasgupta et al. The DevR-DevS and DevR-Rv2027c systems both comprise a histidine protein kinase (DevS or Rv2027c), thus being appropriate as a target of the Hoch invention. By applying the Hoch invention to the DevR-DevS system, it would be obvious that an agent positively identified could be used for tuberculosis or other diseases caused by mycobacteria.

One of ordinary skill in the art would have been motivated to do this because Dasgupta et al. concludes that "the devR-devS two-component system may thus serve as a novel target for

anti-tubercular therapy" (page 158, second paragraph). Tuberculosis is a critical issue, so there is a high incentive to develop or determine compounds for its treatment. There would have been a reasonable expectation of success that the Hoch invention could be used for bacteria such as *M. tuberculosis* that have DevR-DevS and/or DevR-Rv2027c and its homologues based on the fact that Hoch's assay techniques are disclosed as measuring the same reactions catalyzed by Dasgupta's tuberculosis phosphorylases. Finally, it would have been obvious to have expected the same correlation between drug potency and phosphotransfer and radioactivity as recited in claim 1, section c. The degree of phosphotransfer and loss of phosphate-associated radioactivity would have inherently occurred when using the histidine protein kinase system of the claims, as the Hoch reference and the claims under examination use the same processes. In sum, the system of Dasgupta et al. would appear to be just the kind of system that Hoch et al. suggests their methods are applicable for. A holding of obviousness is therefore proper.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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